Annals of Pediatric Surgery

ORIGINAL RESEARCH Open Access

Insertion of central venous catheters in children undergoing bone marrow transplantation: is there a platelet level for a safe procedure?

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Abstract

Background: Bone marrow transplantation (BMT) is a therapeutic procedure for the management of several hematological diseases and malignancies in pediatric population. Central venous catheters (CVCs) play a pivotal role during the process of BMT. The aim of this study was to compare the complications of CVCs placements in children undergoing BMT with platelet levels above and below 50,000/μL and also to detect if there is a platelet count for a safe insertion. This prospective study included all children who had placements of tunneled CVCs during BMT at our hospital between March 2017 and March 2020. Procedures were divided into two groups accordingly to preoperative platelet counts (above and below 50,000/μL). Data were compared between both groups regarding postoperative complications including bleeding or catheter-related blood stream infections (CRBSIs).

Results: Forty-six CVC insertions were performed in 40 patients. There were 20 procedures below 50,000/μL (median 27,500; range 5000–42,000) inserted with perioperative platelet transfusions, and their postoperative levels were median 59,500/μL, range 18,000–88,000. Allogeneic BMT was adopted in 39 patients (97.5%). Beta thalassemia major was the commonest indication (21/40, 52.5%), followed by acute lymphocytic leukemia in six patients (15%). There were nine postoperative complications (bleeding $n = 2$ and CRBSIs $n = 7$) encountered in all placements. Four of them occurred in insertions below 50,000/μL (two bleeding complications that managed conservatively, and two CRBSIs). Post-procedural morbidities regarding bleeding or CRBSIs did not differ significantly between both groups (p value = 0.099 and 0.695, respectively).

Conclusions: Postponement of CVC insertions in thrombocytopenic children due to the fear of potential complications seems unwarranted, as it has no significant impact on the morbidity. Placements of such catheters can be safe under cover of perioperative platelet transfusions irrespective of the preoperative platelet count.

Keywords: Central venous catheters, Children, Thrombocytopenia, Bone marrow transplantation

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The initial result of this study has been presented as an Oral Presentation by the Corresponding Author at the 20th European Pediatric Surgical Association Congress (EUPSA 2019), Belgrade, Serbia.
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Background

Bone marrow transplantation (BMT) is currently considered as a practiced and a well-established modality for the treatment of several hematological diseases and malignancies in children [1]. Central venous catheters (CVCs) have a crucial role in pediatric patients who are undergoing such therapeutic procedure. Their insertions could be effectively used in the infusion of chemotherapeutic drugs, stem cells, blood products, electrolyte supplements, antibiotics, and frequent venous samplings [2, 3].

Considerable numbers of children prior to the process of BMT have severe thrombocytopenia which has been correlated with a high risk of occurrence of morbidities during the placement of CVCs [4]. Some investigators have declared that insertion of these devices could be safely performed in thrombocytopenic patients with a platelet level of 50,000/μL or more without additional perioperative platelet transfusion, in the absence of other coagulation problems [5–7]. On the other hand, some surgeons are usually hesitant regarding CVC insertions in patients with preoperative platelet count less than 50,000/μL due to the fear of occurrence of intra- and postoperative complications. Consequently, there is sometimes a postponement of catheter placements which are essential devices due to the aforementioned purposes [8].

The purpose of this study was to compare the complications of CVC placements in children and adolescents undergoing BMT with platelet levels above and below 50,000/μL and also to detect if there is a platelet count for a safe insertion.

Methods

This is a prospective study that included all children who had placements of CVCs by the dedicated surgical team during the process of BMT at our hospital between March 2017 and March 2020. This study was approved by the institutional review board of pediatric hematology/oncology and BMT unit at our university. A written informative consent was signed by all parents or guardians for the surgical procedure, anesthesia, and data use.

All the included patients had CVC insertions 12 days before the commencement of BMT as per the adopted protocol within our hospital. All procedures were performed in the theater room under general anesthesia and complete aseptic conditions. The internal jugular vein was the preferred site considered for CVC placements in all patients. We always depend on tunneled double-lumen silicone catheters, Hickman or Broviac catheters (Medcomp, Harleysville, PA, USA) accordingly to the availability of sizes. All CVCs were inserted by the guidance of intraoperative ultrasound to avoid arterial puncture, using catheters' sizes ranged from 6 to10 Fr. Intraoperative empirical antibiotic (cephalosporin or clindamycin, if there is allergy to cephalosporin) was administered to all patients. Venous return through the catheter was checked at the end of the surgery, and the line was flushed with heparin to prevent immediate postoperative thrombosis. Plain chest x-rays were conducted after insertions to detect potential occurrence of pneumothorax or hemothorax and to confirm the catheter tip position and the success of the placement. Postoperative careful care of the device was managed by well-trained nurses to avoid thrombosis, infections, and catheter dysfunction.

All procedures were performed by the same standardized operative technique regardless of the preoperative platelet count. The insertions in children within the recommended level of safety (50,000/μL or more) were performed without any platelet transfusion cover. During the procedures in patients who had platelet levels below this threshold, perioperative platelet transfusions were given 2 h before the scheduled placement, and bulky dressing was used after finishing the procedure to compress the surgical site. Postoperatively, complete blood pictures and all coagulation profiles were sampled for further evaluation.

Bleeding complications related to the surgical procedure including puncture-site hemorrhage or hematomas or hemothorax were classified into minor bleeding which does not need any additional surgical intervention and major bleeding which requires surgery to arrest the hemorrhage. Minor bleeding is classified as either grade 1, i.e., oozing is stopped by slight compression, or grade 2, i.e., oozing needs prolonged manual compression to be arrested. Major bleeding is classified into grade 3 and grade 4 that require elective and urgent interventions, respectively [4]. Catheter-related blood stream infections (CRBSIs) were considered when a clinical picture of systemic sepsis was occurred in the absence of a related cause, meanwhile associated with positive and identical bacteria obtained in blood cultures from both a CVC and a peripheral vein [9]. The pathogen count isolated from the CVC should be three times more than that identified from a peripheral venous sampling for a confirmed diagnosis [10, 11]. In the condition of a suspected CRBSI, intravenous baseline antibiotics (gram positive and gram negative) were commenced till the result of the blood culture, in addition to antimicrobial lock therapy that consists of locking catheter with an antibiotic solution while it is not in use. The removal of CVCs was indicated at the end of receiving medications, or in cases with persistent CRBSIs despite administration of the specific antibiotic or in catheter mechanical obstruction unresponsive to the flush with heparinized saline for restoring its patency.

Data were collected from the patients' records and analyzed regarding their baseline criteria, diagnosis, pre- and postoperative platelet levels, other coagulation parameters, perioperative platelet transfusions, types and sizes of CVCs inserted, cause of removal, and complications encountered. The procedures were divided into two groups according to preoperative platelet counts of patients: the first group (group A) included all placements within the safety platelets level (50,000/μL or more), while the second group (group B) contained the insertions below the same level.

Results between both groups were compared using chi-square test in addition to the usual descriptive analysis. The quantitative variables were expressed as mean ± standard deviation [SD]. Statistical significance was accepted when the p value was equal to or less than 0.05. Statistical data analysis was performed using SPSS [Statistical Package for Social Sciences, Version 21.0].

Results

Forty patients were included for analysis, and a total of 46 CVCs were inserted during the series period. There were 31 males (77.5%) and 9 females (22.5%). Mean age at time of the surgical procedure was 5.49 ± 3.59 years (range 2–15 years). Beta thalassemia major was the most common indication for BMT among the included children (21/40, 52.5%), followed by acute lymphocytic leukemia in six patients (15%). Allogeneic BMT was adopted in 39 patients (97.5%), whereas only one child with non-Hodgkin's lymphoma underwent an autologous transplantation.

Preoperative platelet counts for all patients ranged from 5,000 to 505,000/μL with a median of 206,000/μL. Out of all children, 26 (65%) had initial platelet counts above the safety threshold of 50,000/μL, while the other 14 patients (35%) were presented with platelet levels below the same threshold at the time of surgery. All patients underwent CVC insertions, by the same technique, during the preparation for BMT as mentioned previously in the "Methods" section. During the process of BMT, six patients had inevitable device removal; therefore, additional CVCs were placed in such patients who had platelet levels below the safety threshold during the second insertions. Second placements were performed after few days of removal of the catheter as it was the source of sepsis, and also after appropriate course of antibiotics. Consequently, groups A and B included 26 and 20 CVCs placements, respectively. The patients' clinical characteristics in both groups were listed in Table 1.

Median preoperative platelet level in group A was 232,000/μL (range 60,000–505,000). The placements in group B had a median preoperative platelet count of 27,500/μL (range 5000–42,000); of them, there were 8 placements in counts less than 20,000/μL and the remaining 12 were inserted in levels ranged between 25,000 and 42,000/μL. Postoperative platelet counts in group B showed an obvious improvement after preprocedural platelet transfusions; however, 8 out of the 20 procedures still had postoperative platelet levels below 50,000/μL. Other coagulation parameters were within the normal values and did not demonstrate any significant difference between the groups. The comparison between both groups regarding platelet levels and coagulation parameters is shown in Table 2. There were no complications occurred due to platelet transfusions

Table 1 The patients' clinical characteristics in both groups

Parameter	Group A *N* (%)	Group B *N* (%)
Number of patients	26 (65%)	14 (35%)
Number of CVCs insertions	26 (56.5%)	20 (43.5%)
Rt. IJV	26 (100%)	14 (70%)
Lt. IJV	—	6 (30%)
Indication for BMT		
Hematological diseases	26 (100%)	3 (21.4%)
Beta Thalassemia major	21	—
Acquired aplastic anemia	2	2
Sickle-Thalassemia	2	—
Mucopolysaccharaidosis	1	—
Fanconi anemia	—	1
Malignancies	—	11 (78.6%)
ALL	—	6
AML	—	3
Non-Hodgkin's lymphoma	—	2
Perioperative platelet transfusions	—	20 (100%)

CVCs central venous catheters, *IJV* internal jugular vein, *BMT* bone marrow transplantation, *ALL* acute lymphocytic leukemia, *AML* acute myeloid leukemia

Table 2 The comparison between both groups regarding platelet levels and coagulation parameters

Parameter	Group A	Group B
Preoperative		
PT (mean); seconds	12.5	13
aPTT (mean); seconds	32	35.4
INR; mean	1.0	1.1
Platelet count; per microliter		
Range	60,000–505,000	5000–42,000
Median	232,000	27,500
Postoperative		
Platelet count; per microliter		
Range	50,000–430,000	18,000–88,000
Median	220,000	59,500

PT prothrombin time, *aPTT* activated partial thromboplastin time, *INR* international normalized ratio

among the insertions in group B, and also, there were no plasma or coagulation factor transfusions in such group.

Forty CVCs were inserted into the right internal jugular vein, and only 6 were placed in the left side. Regarding the type of CVCs used, Hickman catheters were inserted in 30 placements (65.2%) of all performed procedures, and in the other 16, Broviac catheters (34.8%) were placed. Sixteen placements were of size 9 Fr, followed by 12 insertions of size 6 Fr, and CVC sizes of 7 and 10 Fr were used in the remaining 10 and 8 procedures, respectively.

A total of nine complications were encountered among all insertions; they included 7 CRBSIs and 2 minor bleeding complications. There were no significant statistical difference between both groups regarding bleeding morbidities as only 2 out of the 20 placements in group B developed minor bleeding complications, while there were no bleeding complications in group A (p value = 0.099; hazard ratio 2.444, 95% CI 0.714–3.487). One patient had a hematoma after the procedure and the other had a puncture site hemorrhage, and both were managed conservatively without any surgical intervention. There were no major bleeding complications happened in group B.

Seven CRBSIs were occurred after the first placements at a median time of 21 days post-insertion, with an overall incidence of 17.5% (7/40). The CRBSIs did not achieve a significant difference, as 2 out of 14 patients below the safety level had CRBSIs versus 5 out of 26 patients above the same threshold (p value = 0.695; hazard ratio 1.429, 95% CI 0.239–8.528]. All the encountered CRBSIs were happened with Hickman catheters, and during their course, 14 blood cultures were conducted from both CVC and a peripheral vein. Blood cultures have confirmed that the source of sepsis was the inserted catheter, and they were managed as aforementioned. Regarding the causative organisms in the CRBSIs, there were four, two, and one *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*, respectively. Three devices (one of them was inserted below the safety platelet threshold) were salvaged and passed with uncomplicated CRBSIs, while the other 4 catheters were removed due to resistant infections (*Klebsiella* n = 1, *Staphylococcus epidermidis* n = 1, and *Staphylococcus aureus* n = 2). Moreover, two catheters were removed due to persistent mechanical complications; thus, six patients needed second placements. None of the included patients required a third insertion. There was neither recurrence of CRBSIs nor mortality due to infectious complications.

Discussion

Undoubtedly, CVCs are fundamental tools in the procedure of BMT. They provide the patients with a durable access for irritant parenteral drugs in addition to reduce repeated and painful cannulations [12]. The selection of the device should be based on the indication of placement and the planned duration of use. In our institution, we adopt tunneled external lines which are visible and easy to access with multiple lumens and also no needle stick is required. Despite they are associated with an increased rate of infection when compared to totally implantable ports, their removal could be performed without general anesthesia [13].

CVCs are frequently implemented in patients with hemostatic dysfunction [14]. This study discusses the correlation between platelet levels and potential complications during CVC insertion in children. Several previous reports documented the impact of thrombocytopenia on bleeding-related morbidities in adults [7, 15, 16], while only few studies were conducted among the pediatric population [4, 17, 18]. Josephson et al. reported through an analysis of a clinical trial that bleeding risk is higher and dangerous in children, especially those during BMT, rather than in adults [19]. However, bleeding morbidities in our study were of minor grade (grade 1 = one episode, grade 2 = one episode) that were treated only by observation and manual compression, without any blood component transfusion. One patient who developed local hematoma had severe aplastic anemia with preoperative platelet level of 10,000/μL, and the other with acute lymphocytic leukemia that had postoperative puncture site oozing (preoperative count of 31,000/μL), and after stopping the bleeding, both devices continued in use. Similarly, such event was reported by others in children with malignancies or chronic diseases [4, 17]. The overall incidence of bleeding complications in our series (4.3%) was in a reasonable range when compared to previous pediatric studies that reported 3, 2.5, and 1.1%, respectively [4, 8, 17]. We believe that the slight difference in percentages among studies could be attributed to numbers of the included patients.

The present study demonstrated that preoperative platelet level has no significant correlation with the risk of bleeding-related morbidities after placements of CVCs, and perioperative platelet transfusion can surely reduce such complication. Similar result was also declared by some investigators [4, 17, 18]. On the contrary, Zeidler et al. and Mumtaz et al. reported that associated thrombocytopenia was a risk factor for the occurrence of local hematoma or minor bleeding after device insertion [7, 15].

Bloodstream infection is a prevalent complication after catheter placement in immunocompromised children. The tracing of the source of infection is usually a challenge. CRBSIs occur very early due to imperfect sterile technique during port insertion and considered as a

surgical complication, or later on due to associated risk factors or poor device care [20]. The frequency of CRBSIs among pediatric oncology patients is ranging from 9.8 to 22% [21, 22]. In our study, such rate was 15.2%, and similarly, near results were declared by others in immunocompromised patients with incidence of 17.6, 18.9, and 10.7%, respectively [8, 17, 23]. We did not observe any significant role of thrombocytopenia in relation to the occurrence of CRBSIs. Similarly, our result was in line with previous studies that aimed to assess such factor in children with leukemia [8, 17]. In contradiction, Bamba et al. reported that low preoperative platelet count was a significant risk factor for device infection [20]. Another cohort study revealed that percentage of CRBSIs was equal between patients with platelet levels above and below 50,000/μL after radiological implementation of CVCs [24].

In this study, gram-negative bacteria were the most common organism isolated in episodes of CRBSIs (57%). The predominance of such negative bacilli was also reported previously by other studies involving patients undergoing BMT or with malignancies; Zanwar et al. and Chee et al. showed that 83 and 68% of their cases with CRBSIs were due to gram-negative organisms [23, 25]. Out of all episodes of CRBSIs occurred among our patients, 43% of catheters were salvaged by systemic antibiotics in addition to antimicrobial lock therapy that used as an adjunct modality. Such strategy was also conducted by a recent study, demonstrating a salvage rate of 83% [23], and it was effective towards gram-negative organisms in that study as well as our finding. Eventually, the decision of device removal is critical, and it mainly relies on the clinical course of the infection and the response of the child. The removal should balance between adding another surgical procedure with potential morbidity, meanwhile avoiding deterioration of the patient due to uncontrolled sepsis.

The majority of surgeons adopt a cutoff of 50,000/μL for pre-procedural platelet transfusion during port insertion in both children and adults [4, 20]. A review of practice conducted on adult patients recommended that 20,000/μL should be a safe level, and CVCs could be implemented without perioperative platelet transfusions or potential risks [7]. They also declared that platelet transfusion should be only reserved to patients with levels below 20,000/μL [7]. Evidence-based guidelines are still lacking in the pediatric literature towards this recommendation. Based on the results of this series, we believe that no platelet level is required for safe insertion in children, and empirical platelet transfusions can secure the procedure especially with experienced hands and ultrasound guidance to achieve a one-trial vein cannulation.

Conclusions

Postponement of CVC insertions in thrombocytopenic children due to the fear of potential morbidities seems unwarranted as thrombocytopenia has no significant impact on both, bleeding complications or CRBSIs. Placements of such catheters can be safe in any patient under cover of perioperative platelet transfusions irrespective of the preoperative platelet count, especially with experienced hands under ultrasound guidance.

Abbreviations

CVCs: Central venous catheters; BMT: Bone marrow transplantation; CRBSIs: Catheter-related blood stream infections; SD: Standard deviation; SPSS: Statistical Package for Social Sciences

Acknowledgments

The authors gratefully thank Mr. Ahmed Samir Ryad for the technical assistance in the manuscript.

Authors' contributions

Study design: AE; Data collection: EE; Data analysis: AE; Manuscript writing: AE; Manuscript critical review: AE; The authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on a reasonable request.

Ethics approval and consent to participate

This study was approved by the institutional review board and research ethical committee of pediatric hematology/oncology and BMT unit at the Faculty of Medicine, Tanta University, with an approval number of 14726/01/17. A written consent was obtained from all study participants.

Consent for publication

Written informed consents were signed by all parents for surgery and data use in scientific purpose only at the time of management at our center. This consent was clearly stated in the manuscript in the "Methods" section. All private data of patients such as name, address, and phone number or even identity photos will not appear in the research. The consents are in the patients' medical records.

Competing interests

The authors declare that they have no competing interests.

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Received: 27 July 2020 Accepted: 20 October 2020
Published online: 30 November 2020

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